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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.		
10/510,628	05/09/2005	Peter Hegemann	231181	4179		
23460	7590	05/07/2008	EXAMINER			
LEYDIG VOIT & MAYER, LTD TWO PRUDENTIAL PLAZA, SUITE 4900 180 NORTH STETSON AVENUE CHICAGO, IL 60601-6731				MACFARLANE, STACEY NEE		
ART UNIT		PAPER NUMBER				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/510,628	HEGEMANN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 14 February 2008.

2a) This action is **FINAL**.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-5, 8-26 and 32-35 is/are pending in the application.

4a) Of the above claim(s) 13-18 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-5,8-12,19-26 and 32-35 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date _____ .	6) <input type="checkbox"/> Other: _____ .

## **DETAILED ACTION**

### ***Response to Amendment***

1. Claims 1-5 and 8-26 have been amended, claims 6-7 and 27-31 are cancelled, and claims 32-35 have been newly added as requested in the amendment filed on February 14, 2008. Following the amendment, claims 1-5 and 8-35 are pending in the instant application.

Claims 13-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper filed on November 1, 2007.

Claims 1-5, 8-12, 19-26 and 32-35 are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3. Applicant's arguments filed on February 14, 2008 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

### ***Sequence Compliance***

4. Claim 8 stands objected to for containing sequence disclosures that are encompassed by the definitions for amino acid sequences set forth in 37 C.F.R. § 1.821 (a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825, for reasons of record as set forth in the previous Office

Action dated December 19, 2007. Specifically, no sequence identifier has been provided for the amino acid sequences presented in Claim 8. It appears that applicant is attempting to reference several distinct sequences: LDXXXKXXW, IDXXXKXXW, LDXXXKXXF, LDXXXKXXY, IDXXXKXXF, and IDXXXKXXY, each of which needs a sequence identifier. In case these sequences are new, Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO: ) be made in the specification and claims wherever a reference is made to that sequence. See M.P.E.P. 2422.04.

***New Grounds of Rejection – Necessitated by Amendment***

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-5, 8-12, 19-26 and 32-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 1, 21 and 22 are vague and indefinite in their recitation of "alter". The term "alter" is a relative term which renders the claim indefinite. The term "alter" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

8. Claim 1 is vague in its recitation of a photoreceptor that is "configured to act as a light-controlled ion channel". The claim appears to be incomplete for omitting essential method steps, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted steps are: the method does not recite any active steps by which the photoreceptor is configured to act as a light-controlled ion channel. Absent said recitation the claim limitation potentially raises issues under 35 USC 112, enablement requirement, as to how one of ordinary skill in the art would practice the claimed method.

9. Claims 25 and 26 are vague in their recitation of "the intracellular concentration of ions across the membrane". It is unclear if Applicant is claiming the intracellular concentration or the ratio of intracellular versus extracellular concentrations. One of ordinary skill in the art would not be reasonably apprised as to how the concentration can be both "intracellular" and "across the membrane".

10. Claim 35 is vague and indefinite in its recitation of “wherein a light-induced membrane depolarization is realized”. The claim appears as incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the active step by which the depolarization is determined. At present the claim reads upon a step that occurs by mental action, which is non-statutory subject matter. Absent an active step by which the depolarization is detected, the claim raises potential issues under the requirement for enablement, because one of ordinary skill in the art would not be reasonably apprised as to how to perform the invention as claimed.

11. Claims 2-5, 8-12, 19-20, 23, 24 and 32-34 are indefinite for depending from an indefinite claim.

#### ***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

13. Claims 1-5, 19-23 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Hildebrant et al., *PNAS, USA* 90:3578-3582, published April 1993, as evidenced by Wald G., *Nature*, 219(5156): 800-807, published August 24, 1968.

14. Claims 1 is drawn to a method for altering the ion conductivity of a membrane, comprising inserting one or more biological photoreceptors into a membrane wherein the photoreceptor is an apoprotein and a light-sensitive polyene covalently bound to the apoprotein and functioning as a light-sensitive gate thereby altering ion conductivity. Dependent claims recite wherein the apoprotein is a transmembrane protein with 5 or more transmembrane helices (claim 2); wherein the ion channel is a proton, sodium or calcium ion channel (claim 3); wherein the apoprotein is an opsin or derivative of the natural amino acid sequence (claims 4 and 5); wherein the polyene is a retinal or derivative (claims 19 and 20); wherein the proton, sodium or calcium conductivity is altered (claim 21); the membrane potential of the cell is altered (claim 22); the membrane is a cell membrane of yeast (claim 23); and wherein the yeast is *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, or *Pichia pastoris* (claim 32).

15. The Hildebrant prior art teaches the heterologous expression of bacteriorhodopsin in yeast membranes of *Schizosaccharomyces pombe*. Bacteriorhodopsin is an opsin protein and the reference teaches expression of the natural amino acid sequence. Bacteriorhodopsin is known in the art as a seven transmembrane receptor and the reference teaches expression in yeast with the presence of the chromophore retinal (abstract). The Wald reference teaches that binding of retinal to opsin leads to the formation of a covalent Schiff base. Furthermore, the Hildebrant reference teaches the detection of altered ion conductivity, namely that of protons, as well as altered membrane potential (Figures 3, 5 and 7). Thus, the reference anticipates the method of claims 1-5, 19-23 and 32.

16. Claims 1-5, 8-12, 19-22 and 35 rejected under 35 U.S.C. 102(a) as being anticipated by Nagel *et al.*, (2002), cited as reference AD on the IDS filed November 2, 2004.

17. Claims 1 is drawn to a method for altering the ion conductivity of a membrane, comprising inserting one or more biological photoreceptors into a membrane wherein the photoreceptor is an apoprotein and a light-sensitive polyene covalently bound to the apoprotein and functioning as a light-sensitive gate thereby altering ion conductivity. Dependent claims recite wherein the apoprotein is a transmembrane protein with 5 or more transmembrane helices (claim 2); wherein the ion channel is a proton, sodium or calcium ion channel (claim 3); wherein the apoprotein is an opsin or derivative of the natural amino acid sequence (claims 4 and 5); wherein the apoprotein has the consensus sequence LDXXXXKXXW (claim 8); wherein the apoprotein is derived from lower plants (claim 9); wherein the lower plants are algae (claim 10); wherein the apoprotein is an opsin from *Chlamydomonas reinhardtii* (claim 11); wherein the apoprotein includes at least amino acids 61-310 of SEQ ID NO: 1 (claim 12); wherein the polyene is a retinal or derivative (claims 19 and 20); wherein the proton, sodium or calcium conductivity is altered (claim 21); the membrane potential of the cell is altered (claim 22); wherein a light-induced membrane depolarization is detected (claim 35).

18. The Nagel et al. reference teaches heterologous expression of channelrhodopsin-1 (Chop-1) which is encoded by the amino acid sequence of SEQ ID NO:1 in *Xenopus* oocytes in the presence of all-trans retinal (page 2395, paragraph

2). The reference states that the protein has the consensus motif LDXXXXXXW (page 2395, paragraph 1), thus teaching the requirement of claim 8. Nagel et al. further report the detection of light-induced membrane depolarizations (Figure 2A) and ion transport under voltage-clamp conditions (Figure 2B). Specifically, the reference recites altered light-induced ion conductance and ion replacement and sensitivity studies lead Nagel et al. to conclude that the photocurrent is carried by protons (paragraph bridging pages 2395 and 2396). Thus, the Nagel reference anticipates the limitations of instant claims 1-5, 8-12, 19-22 and 35.

***Conclusion***

19. No Claim is allowed.
20. This application contains claims drawn to an invention nonelected with traverse in Paper filed on November 1, 2007. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M,W and ALT F 7 am to 3:30, T & R 5:30 -5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane  
Examiner  
Art Unit 1649

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Primary Examiner, Art Unit 1649